

## MENINGOMYELITIS AND MYELITIS—38 CASES.

Disorder of size, shape and contour of pupils . . . . .	30
Loss of light reflex . . . . .	17
Changes in optic nerve . . . . .	1
Evidence of third-nerve involvement . . . . .	4
Evidence of fourth-nerve involvement . . . . .	0
Evidence of sixth-nerve involvement . . . . .	2

## CEREBRAL MENINGITIS—20 CASES.

Disorder of size, shape and contour of pupils . . . . .	20
Loss of light reflex . . . . .	14
Papilledema . . . . .	5
Optic atrophy . . . . .	8
Third-nerve involvement . . . . .	6
Fourth-nerve involvement . . . . .	1
Sixth-nerve involvement . . . . .	4

## SYMPTOMATIC DIAGNOSIS—37 CASES.

Disorder of size, shape and contour of pupils . . . . .	24
Loss of light reflex . . . . .	13
Evidence of second nerve involvement . . . . .	1
Evidence of third-nerve involvement . . . . .	5
Evidence of fourth-nerve involvement . . . . .	0
Evidence of sixth-nerve involvement . . . . .	1

## CARDIAC SYPHILIS.

By WILLIAM CABELL MOORE, B.A., M.D.,

ASSOCIATE IN MEDICINE, GEORGE WASHINGTON UNIVERSITY,  
WASHINGTON, D. C.

SYPHILIS has been recognized as a cause of heart disease for several centuries, and for a long time has been thought to be an important factor in the production of arteriosclerosis and aneurysm; but until recent years heart disease was not thought to be a frequent complication of syphilis, nor has the nature of syphilitic infection of the heart been correctly understood. During the last six to eight years, however, this subject has been studied more thoroughly, and medical literature has contained a great many articles pertaining to it. In the main these articles have dealt with syphilis of the aorta rather than syphilis of the heart, but, judging by Warthin's studies,<sup>1</sup> syphilis of the heart occurs quite as frequently, if not more frequently, than syphilis of the aorta, and it would even appear that the heart is syphilitic in every individual showing good evidence of syphilis elsewhere, and possibly in some showing no gross evidence whatever of the disease.

In 1909 Wright and Richardson<sup>2</sup> demonstrated the *Spirocheta pallida* in the aortas of 5 cases of syphilitic aortitis, in every one of which the aortic valves showed more or less well-marked fibrous

changes; in 1914 Cabot,<sup>3</sup> in proposing a new classification of cases with failing heart, called one of the four types "syphilitic;" in 1915 Anders<sup>4</sup> states that rheumatism and syphilis head the list as causes of heart disease, and that some recent investigators say syphilis is the principal factor; while more recently Warthin<sup>5</sup> reports that in the pathological service of the University of Michigan, from 1912 to 1914, one-third of all the autopsy cases on adults (41) showed active syphilis on microscopic examination, of which lesions were found in the heart in 88 per cent.

Formerly these cardiac lesions were supposed to belong only to the tertiary and later stages. The lesions were thought to be mainly gummata or aneurysms or some less well-defined disease. But since the discovery of the *Spirocheta pallida* as the cause of syphilis, and of methods of staining the spirochetes in tissue, and of the Wassermann reaction as an aid to diagnosis, it has been learned that the heart may be affected in both the secondary and tertiary stages of the disease, and that the lesions are more frequently an epicarditis, endocarditis, or myocarditis.

The spirochetes appear to have a special affinity for the heart and aorta, and are found frequently in these organs in syphilis. Renter<sup>6</sup> and Benda<sup>7</sup> and Schmorl,<sup>8</sup> in Europe, first reported finding the spirochetes in the wall of the aorta in 1906 and 1907 and Wright and Richardson,<sup>2</sup> in this country, in 1909. Since then many others have confirmed these reports. However, Larkin and Levy<sup>9</sup> consider the demonstration of spirochetes in specimens of syphilitic aortitis as doubtful, and Longcope,<sup>10</sup> who has made a careful study of syphilitic aortitis, said several years ago that spirochetes could not be demonstrated in such lesions constantly by any means. Warthin's<sup>5</sup> painstaking and accurate studies and reports, however, prove conclusively that they can be so demonstrated, and in the tissues of both the heart and aorta. He reported last year finding the spirochetes or the characteristic tissue lesions in the hearts of a number of latent, active, and unsuspected cases of syphilis that came to autopsy, and thus pointed out the relative frequency of syphilis of the heart, as just mentioned. He found syphilis of the heart in 88 per cent. of syphilitics, while the aorta was found involved in only 78 per cent., which is contrary to the prevailing idea heretofore.

Warthin<sup>11</sup> also reported, in 1911, finding the heart wall crowded with spirochetes in congenital syphilis in nine infants and young children that came to autopsy. In eight of these syphilis was not even suspected clinically. Up to this time congenital syphilis of the heart was considered a rarity, being limited to those cases in which gumma of the heart was found; but Warthin showed that there exists a special form of diffuse interstitial myocarditis in congenital syphilis, with nothing in the gross appearance to suggest myocarditis, but with certain fibroblastic epithelioid areas of the heart wall microscopically found crowded with spirochetes. Warthin considers this

an important cause of sudden death in early life, occurring as a rule in apparently healthy children, in whom syphilis may never have been suspected clinically. In this connection Wiesner,<sup>12</sup> in 1905, reported finding syphilitic aortitis in congenital syphilitics, and Rach and Wiesner,<sup>13</sup> in 1907, found changes in the aorta in the majority of a large number of syphilitic fetuses examined; while Klotz,<sup>14</sup> in 1908, found lesions in the aorta, practically identical with those in the acquired disease, in a case of congenital syphilis that came to autopsy.

As to the nature of the syphilitic process in the heart, various authorities<sup>9 10 16 17 18</sup> practically agree that the lesion begins in all stages in the lymph spaces around the small vessels as a localized or diffuse, perivascular, small round-cell and plasma-cell infiltration, resulting in a productive inflammatory process. The evidence of these changes is plain microscopically, where there may be little or no macroscopic evidence, and the spirochetes may be found in these areas at autopsy.<sup>5 13 19</sup> Likewise, this process can be differentiated histologically from the simple degenerative process in atherosclerosis.<sup>9 15</sup>

The lesion may be situated in the epicardium, the endocardium, or the myocardium, but is more frequently found in the myocardium. In a series of 50 cases that came to autopsy, reported by Brooks<sup>16</sup> in 1913, the myocardium was diseased in 44 cases and the epicardium in 28, disease of the coronaries occurred in 35, and there was cardiac gumma in 5. Brooks does not mention the number in which endocarditis was present, but syphilitic endocarditis is known to occur frequently, and syphilis is such a well-known factor in the production of aortic endocarditis that it is to be suspected strongly in any case of aortic insufficiency. This is the most frequently encountered syphilitic valvular lesion, and occurring without involvement of any other valve, especially in patients under fifty, is extremely suggestive of syphilitic origin. Longcope,<sup>10</sup> basing his deductions upon a series of autopsy cases, found that 81.5 per cent. of cases of uncomplicated aortic insufficiency were probably syphilitic, and Larkin and Levy<sup>9</sup> state that pure aortic insufficiency is undoubtedly of syphilitic origin except in cases of infective endocarditis. When the aortic lesion is associated with a lesion of the mitral or of other valves, syphilis is less likely to be the cause, the probable origin being an infective or atheromatous process; but syphilis should be suspected until disproved. Longcope<sup>20</sup> has reported 2 cases of aortic insufficiency associated with disease of the mitral valves in which the Wassermann reaction was positive, but he states that spirochetes were not found in the mitral valves, and therefore the mitral lesion was not proved positively to be syphilitic.

Aortic insufficiency is also often associated with aortitis and sometimes with aneurysm of the arch of the aorta, both frequently the result of syphilis. Wright and Richardson<sup>2</sup> found involvement of

the aortic valve in the 5 cases in which they found spirochetes in the aorta; Larkin and Levy<sup>9</sup> state that an insufficient aortic valve is the most common complication of syphilitic aortitis, and Longcope<sup>10</sup> has frequently found the two associated, the general impression being that the valvular lesion is an extension from the aortitis. Longcope<sup>12</sup> found 4 cases of aneurysm in 43 cases of aortic insufficiency, and a similar case was seen by me within the past month at the George Washington Hospital Dispensary: A colored woman, aged twenty-eight years, with the physical signs of aortic insufficiency, and a broad supracardiac area of dulness which the fluoroscope showed to be a pulsating and expansile mass. She had a strongly positive Wassermann.

Also, lesions of other valves than the aortic are sometimes found associated with aortitis, or with aneurysm of the arch, in patients with a positive Wassermann and other evidences of syphilis, who do not give a history of rheumatism or other infection, except syphilis, that might produce endocarditis. Two such cases have been seen by me recently. In one, seen in the George Washington Hospital Dispensary, there were the signs of mitral stenosis and of aortitis in a woman, aged thirty-one years, who had a positive Wassermann and syphilitic sores in the mouth. In the other, seen in the hospital wards, there was a pulmonary stenosis associated with a beginning aortitis in a syphilitic, in whom the valvular lesion appeared to be the result of an acute endocarditis, and therefore of recent origin. If so the inference is that it was due to syphilis, though there was no absolutely definite evidence to this effect. This patient was seen by other observers, all of whom concurred in the diagnosis of pulmonary stenosis. Pulmonary stenosis is found so rarely in acquired cardiac disease that this case should be of sufficient interest to be reported briefly.

CASE REPORT.—II. II., aged twenty-eight years; white; male; married; cashier in a restaurant. This patient was sent in by Dr. Kane because of fever, headache, vertigo and nausea setting in suddenly three days before. His family history and personal history were negative. He denied syphilitic infection, but his Wassermann was four plus and Noguchi two plus. He had been married nine months and his wife had become pregnant once, resulting in a miscarriage. His temperature was irregular, ranging the first three days from 97.6° to 104.6°; the next two weeks from 98° to 101°; and then for four days from 98° to 100°, which it was when he left the hospital. Examination disclosed nothing to account for the fever other than the cardiac findings and the positive Wassermann. There was no throat or joint involvement that could be made out, nor history of any at a previous time. The cardiac impulse was in the fifth left interspace, 11 cm. from the midsternum, and the R. C. D. extended 12 cm. to the left and 3 cm. to the right of the midline. There was an area of retromanubrial dulness extending

5 em. to the left and 2 em. to the right in the first interspace, and 3.5 em. to the left and 2 em. to the right in the second interspace. There was a marked systolic thrill felt in the first, second and third spaces to the left of the sternum, most marked in the first. A soft systolic murmur was heard at the apex and transmitted faintly to the axilla; a loud, long, and coarse systolic murmur was heard over the left base, loudest in the first left space, also a faint systolic murmur was heard in the aortic space and in the neck. These murmurs and the thrill were scarcely recognizable at the first examination, later increased in intensity, and varied much in intensity from time to time. The aortic second was distinct, the pulmonary second faint. The blood-pressure was 124 systolic and 64 diastolic in the left arm and 126 systolic and 58 diastolic in the right arm (Tyco). The pulse was regular in force and frequency, 64 to 100, generally between 80 and 90. There was no tracheal tug and pulsation in the radials was synchronous. The blood, on admission, showed 80 per cent. hemoglobin, 4,200,000 red cells, and 8900 leukocytes; 65 per cent. polymorphonuclear neutrophils and 4 per cent. eosinophils, 10 per cent. small and 20 per cent. large lymphocytes, and 1 per cent. transitionals. One week later there were 11,200 leukocytes. The Widal was negative and the malarial parasite was not seen in four examinations. A roentgen ray by Dr. J. H. Selby showed an area of increased density in the first and second spaces, comparing accurately with the area of dullness in this region, and the fluoroscope showed no expansile tumor. He was given one deep injection of salicylate of mercury, which produced salivation promptly, and two doses of salvarsan, but did not seem to be particularly benefited. He left the hospital at his own request, and, unfortunately, has been lost sight of.

The time at which the heart lesion becomes manifest varies and cannot always be determined, but Brooks<sup>16</sup> states that serious involvement of the heart may begin before or with the secondary stage, and that lesions in the heart frequently appear early. In one case in Brook's series death resulted from a minute perforation of the aorta just above the ring before the secondary rash had fully appeared and before the diagnosis had been made. Other instances of early cardiac syphilis have been recorded, but not many. In this connection I wish to mention a case recently seen by me:

A young man, aged twenty-four years, referred by Dr. Garnett for examination because of precordial pain of a few days' duration, had a temperature of 99.6° and a pulse rate of 110, a slightly enlarged area of cardiac dullness, an occasional extrasystole and a soft systolic murmur at the base. There was a beginning macular eruption over his body, which he had not noticed until it was pointed out to him at that time. He denied knowledge of luetic infection, but acknowledged possible exposure to infection. His Wassermann was strongly positive. Since getting antiluetic treatment his

cardiac symptoms have subsided. Therefore this would appear to be a case of syphilis with cardiac involvement occurring early in the secondary stage.

The cardiac involvement is not often recognized at this early stage, however. The majority of cases of cardiac syphilis are discovered at a later period, owing, probably, to the fact that the symptoms of cardiac syphilis in the early stages are not very definite, and to the fact that the relation between such cardiac symptoms and syphilis is not generally understood. Possibly, too, though infection of the heart occurs early, the process may remain latent for years.

Precordial pain, palpitation, dyspnea, tachycardia, with intermittence, extrasystole or other disturbance of rhythm, more marked on slight exertion, together with a soft systolic murmur at the apex, are very suggestive of cardiac involvement even when history of the infection is denied. Grassman,<sup>21</sup> in his study of the vascular system of 288 cases of secondary syphilis, states that in 85 per cent. there were disturbances in the rate and rhythm of the pulse, while accidental murmurs, usually with dilatation of the heart, occurred in 40 per cent. With the secondary stage, in addition to the symptoms directly referable to the heart, there also are symptoms of a mildly acute infectious disease, slight fever with a moderate leukocytosis often and a relative polymorphonuclear increase. Later in the disease, after a longer cardiac involvement, the earlier cardiac symptoms having been overlooked possibly, the symptoms are those of an acute or more usually a chronic endocarditis, generally of the aortic valve; or of myocarditis; or of angina, due possibly to partial occlusion of the coronary arteries; or of heart-block.

The diagnosis will depend upon these signs and symptoms of some cardiac disorder, together with the history, the general aspects of the case, the Wassermann, and the response to specific medication. Possibly the most important single element is a positive Wassermann. In a study of 36 cases of aortic disease, in 1912, Cummer and Dexter<sup>22</sup> found a positive Wassermann in 27, or 75 per cent.; and out of 47 cases examined by Longcope<sup>10</sup> 35, or 74.4 per cent., gave a positive reaction. Seven of these positive cases came to autopsy, and all showed typical mesaortitis with involvement of the aortic ring, while in 3 spirochetes were found in the wall of the aorta. Larkin and Levy<sup>9</sup> state that 94 per cent. of individuals with luetic aortitis give a positive Wassermann. Similar reports are to be found, the percentage of positive Wassermans being variously given. Longcope,<sup>10</sup> in summing the matter up, gives from 25 to 68 per cent. positive in general cardiovascular disease, from 75 to 80 per cent. positive in aortic insufficiency, from 85 to 95 per cent. positive in aneurysm, and from 75 to 88 per cent. positive in aortic disease in general. As stated before, the signs of aortic insufficiency, unassociated with other valvular lesions, in an individual under fifty are practically pathognomonic of cardiac syphilis, when

infective endocarditis can be excluded; and the association of any valvular lesion with an aortitis or an aneurysm of the arch of the aorta in a person with a positive Wassermann, in whom rheumatism can be excluded, is, to my mind, to be looked upon with great suspicion. Anginal attacks suggest disease of the coronaries or cardiac aneurysm, and the possibility of syphilitic etiology in this event, especially in persons under fifty, should be carefully investigated. The so-called cardiac crises in tabes are probably anginal attacks from coronary disease, so frequently the result of syphilitic infection of these vessels. Warthin<sup>8</sup> believes that the heart and aorta of every latent syphilitic are involved, and that syphilis will be found to be the principal factor in the production of myocardial insufficiency and the cardiovascular renal complex. From his studies it is to be inferred that when syphilitic aortitis exists there exists also syphilitic involvement of the heart, and, also, contrary to the general impression, that the cardiac lesion is not necessarily incidental to the aortitis. This aortitis may be recognized by increased retromanubrial dullness, a broad roentgenographic shadow in this region, possibly increased systolic blood-pressure, a systolic murmur at the base transmitted to the neck as a rule, and a positive Wassermann.

A cure of cardiac syphilis is hardly to be expected under any circumstances, but an amelioration of the symptoms and a prolongation of life in comparative comfort may be expected when proper treatment is instituted early. Even in late cases proper treatment will do much good, but after cardiac decompensation has set in it is unusual for any treatment to do more than slight good, and such cases usually end fatally within a comparatively short time. There were 2 cases with decompensation in the George Washington University Hospital wards recently. One derived no benefit from any treatment and ended fatally in a short time; the other improved somewhat under rest, digitalis, mercury, and salvarsan, and left the hospital, but was never able to return to work, and has again more recently returned to the hospital for further treatment. Brooks and Carroll<sup>17</sup> state that when treatment has been interrupted, as in this instance, and is later resumed again, one rarely gets as prompt and satisfactory a response. This observation is exemplified in this patient.

Treatment of cardiac syphilis should be mainly antisyphilitic and intensive. It should differ but little, if at all, from the treatment of syphilis generally, except in so far as the cardiac involvement may be seen to be affecting the patient. The principal object should be to destroy the spirochetes in the tissues as quickly and as effectively as possible, and therefore antisyphilitic treatment should be pushed to the limit of tolerance. As to specific medication, there can be no cut-and-dried rules that will apply to all cases. Each case must be treated individually. Mercury by deep injection, preferably

one of the soluble salts, and salvarsan intravenously are both to be used. There appears to be but little choice between the old and the new salvarsan, but personally, from a rather limited observation, I am inclined to prefer the old. There is some question as to the use of salvarsan in acute endocarditis, but used in small dose often repeated, rather than in full dose, I believe it to be safe. The iodides are apparently of no use in the early cases, though possibly helpful in old lesions. Improvement is prompt, as a rule, in all cases, though, of course, more marked in early cases, and cardiac decompensation always offers a poor prognosis. In the early cases the patients must avoid cardiac strain until their cardiac symptoms are in abeyance; otherwise cardiac treatment is not indicated. In long-standing cases, when circulatory disturbance is more marked, improvement often takes place promptly under specific treatment alone, but, as a rule, it is almost always advisable also to place these patients under the usual hygienic and therapeutic treatment indicated by the circulatory condition, mainly rest and digitalis.

According to Brooks and Carroll, Anders and others treatment should be continued for at least one year after all signs of activity have subsided, and, irrespective of a negative or a positive Wassermann, antispecifics should be administered from time to time throughout life.

**CONCLUSIONS.** Cardiac complications during syphilis occur much more frequently than has been recognized generally heretofore.

The cardiac lesions occur earlier in the disease than has been thought, even in the early secondary stage.

Congenital syphilis of the heart is a cause of sudden death in early life, this condition being unsuspected clinically, as a rule.

The nature of the process in the heart is distinct and may be recognized microscopically, and the spirochetes may be found in the lesion; it is most frequently a myocarditis. Uncomplicated aortic insufficiency is of syphilitic origin in the majority of instances.

The symptoms are not definite but extremely suggestive; the diagnosis depends mainly upon the signs of some cardiac disorder, with a positive Wassermann, and a response to antiluetic treatment.

The prognosis is good in the early stages and varies directly with the stage of the disease and the extent of the changes produced.

Treatment should be mainly antisiphilitic and intensive. Cardiac treatment is required rarely except in cases with decompensation. Once instituted treatment should be carried through persistently and uninterruptedly.

#### REFERENCES.

1. Warthin, A. S.: *Tr. Assn. Am. Phys.*, 1914, p. 416.
2. Wright and Richardson: *Boston Med. and Surg. Jour.*, 1909, cli, 539.
3. Cabot, R. C.: *Jour. Am. Med. Assn.*, 1914, lxxiii, 1461.
4. Anders, J. M.: *AM. JOUR. MED. SC.*, 1915, cl, 835.
5. Warthin, A. S.: *AM. JOUR. MED. SC.*, 1916, clii, 508.



6. Reuter: München. med. Wehnschr., 1906, liii, 778.
7. Benda: Berlin. klin. Wehnschr., 1906, xliii, 989.
8. Schmorl: München. med. Wehnschr., 1907, liv, 188.
9. Larkin and Levy: Jour. Exper. Med., 1916, xxiii, 25.
10. Longcope, W. T.: Arch. Int. Med., 1913, xi, 15.
11. Warthin, A. S.: Am. Jour. Med. Sc., 1911, cxli, 398.
12. Wiesner, R.: Centralbl. f. Path. u. path. Anat., 1905, xvi, 822.
13. Rach and Wiesner: Wien. klin. Wehnschr., 1907, xx, 521.
14. Klotz, O.: Jour. Path. und Bacteriol., 1908, xii, 11.
15. Longcope, W. T.: Jour. Am. Med. Assn., 1910, liv, 118.
16. Brooks, H.: Am. Jour. Med. Sc., 1913, cxlvi, 513.
17. Brooks and Carroll: Jour. Am. Med. Assn., 1914, lxviii, 1456.
18. Fordyce, J. A.: Am. Jour. Med. Sc., 1915, clxix, 761.
19. Warthin, A. S.: Am. Jour. Med. Sc., 1914, cxlvii, 667.
20. Longcope, W. T.: Bull. Ayer Clin. Lab., 1910, p. 60.
21. Grassmann, C.: Deutsch. Arch. f. klin. Med., 1900, lxxviii, 455; and 1901, lxxix, 58 and 261.
22. Cummer and Dexter: Jour. Am. Med. Assn., 1912, lix, 412.

## SULPHOCONJUGATION AS A TEST OF LIVER FUNCTION.

By MAX KAHN, M.D., Ph.D.,

NEW YORK.

(From the Department of Laboratories, Beth Israel Hospital, New York.)

Of the various functions of the liver, its detoxicating influence is one of the most important, and one also, to which very much attention has been devoted. It is quite well known that toxic radicals liberated during the process of normal or abnormal intestinal digestion are carried to the liver by means of the portal circulation, and there either neutralized or oxidized or conjugated, etc., to lessen or remove the toxic influence of the substance. One of these methods of detoxication is the union of aromatic radicals with sulphuric acid and their excretion in the form of conjugated sulphates (etheral sulphates) in the urine.

Since Städeler found phenol in cows' and horses' urine, Landolt, Lieben, Hoppe-Seyler, Buliginsky, and Munk found traces of it in normal human urine, and Salkowski observed that in ileus and other obstructive intestinal disease the excretion of phenol in the urine is much increased.

This formation of phenol and phenolic substances, cresol, indol, skatol, etc., has been ascribed to the action of intestinal bacterial flora. Such organism like the *B. coli communis*, which is a normal inhabitant of the intestinal canal, are harmless under ordinary circumstances. In conditions of injury to the intestinal mucosa these organisms become virulent (Fermi and Salto). Other organisms, like the *B. putrificus*, the *B. aerogenes capsulatus*, which are obligatory anaerobes, thrive in the colon when there is no oxygen (Herter) and break up protein into the carbocyclic, toxic substances.